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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,926	04/16/2001	Peter Pochlauer	2001_0331A	5439

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EXAMINER

ZUCKER, PAUL A

ART UNIT

PAPER NUMBER

1621

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/834,926

Applicant(s)

POCHLAUER ET AL.

Examiner

Paul A. Zucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-14 and 16-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-14, 16-21 and 23 is/are rejected.
- 7) ☒ Claim(s) 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. In view of the Appeal Brief filed on 7 March 2003, PROSECUTION IS HEREBY REOPENED. New rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

- (1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,
- (2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Current Status

2. This action is responsive to Applicants' Appeal Brief of 7 March 2003 in Paper No 12.
3. Receipt and entry of Applicants' Appeal Brief is acknowledged.
4. Claims 11-14 and 16-23 remain pending.
5. The rejection under 35 USC § 103(a), second paragraph, set forth in paragraph 7 of the previous Office Action in Paper No 8 is withdrawn in favor of the new rejection below. Applicants' remarks with regard to that rejection are therefore rendered moot

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but have been carefully considered and are taken into consideration in the new rejection below.

New Rejections

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 11-14, 16-21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collet et al (Bulletin de la Société Chimique de France 1973, 12, Pt. 2, pages 3330-3334, English translation, pages 1-18) in view of Effenberger et al (US 4,859,784 08-1989).

Instantly claimed is a process for the purification of (R) and (S) - α -hydroxycarboxylic acids which consists essentially of recrystallizing impure acids in a hydrocarbon solvent optionally in the presence of a co-solvent. The source of the hydroxycarboxylic acid, as claimed, is an enzyme-catalyzed addition of cyanide ion.

Collet teaches (Translation, page 15, lines 1-11 and page 16, lines 6-11) the production of each antipode of o-bromo and o-chloro mandelic acid in optically pure form (100% ee) via the decomposition of the ephedrine salts and recrystallization of the resulting hydroxy acids from benzene. Collett teaches (Translation, page 15, lines 7-11), for example, that the rotation of the (+)-o-chloromandelic acid can be improved from an initial value of +57° to a value of +159° for the optically pure

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(100% ee) material by recrystallization from benzene. The recrystallization also removes any trace of the ephedrine salt resulting in an increase in chemical as well as optical purity.

The difference between the instantly claimed process and that taught by Collet is that Collet teaches (Translation, page 11, line 24- page 12, line 14) producing the mandelic acids by the hydrocyanation of the corresponding benzaldehydes in the presence of acid followed by resolution while in the instant case an enzyme catalyzed process is employed. (NOTE; Collett also teaches use of benzene as a recrystallization solvent to increase the chemical purity of the racemic hydroxy acids)

Effenberger, however, teaches (Column 1, line 66- Column 3, line 11) a method for the synthesis of optically active cyanohydrins via the reaction of an aromatic aldehyde with hydrocyanic acid in the presence of the enzyme D-oxynitrilase as a catalyst. Effenburger teaches (Column 2, lines 52-65) the use the use of a large variety of solvents and their mixtures. Aromatic hydrocarbons (Column 2, lines 52-56) are taught as solvent and the presaturation with water or an aqueous buffer corresponding to the instant co-solvent is also taught (Column 2, line 66- column 3, line 7). Effenberger further teaches (Column 2, lines 52-65) the use of t-butyl methyl ether as a reaction solvent. The amount of water in the water-saturated aromatic solvent is considered to fall within the limits of instant claim 19. Effenberger specifically teaches (Column 2, line 16) the use of o-chlorobenzaldehyde in the process. This corresponds to the intermediate required for synthesis of 2-

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chloromandelic acid (cf. instant claim 14). Effenberger exemplifies (Column 3, line 49 – column 4, line 54) the cases of benzaldehyde, o- and m -methoxybenzaldehyde which proceed with diastereomeric excesses of 99.3, 90 and 98%, respectively, for the crude product cyanohydrins. Effenberger is silent with regard to the process for conversion of the product cyanohydrins into optically active 2-hydroxycarboxylic acids but does specifically suggest (Column 3, lines 15-19) that the crude solutions of cyanohydrins can be directly converted into optically active 2-hydroxycarboxylic acids:

“It is not necessary that the crude solutions be purified or treated any further, but can be directly used in further processes under certain conditions, for instance by hydrolysis into the corresponding optically active 2-hydroxycarboxylic acids.”

Since aromatic hydrocarbons are taught as solvents the instantly claimed direct recrystallization is obvious in light of Collett's teaching.

It would have been obvious to substitute the improved method for the enzyme-catalyzed production of mandelic acids of Effenberger for the classical hydrocyanation of Collet. The instantly claimed process would therefore have been obvious to one of ordinary skill in the art. The motivation would have been to use the method of Effenberger to produce optically enriched 2-hydroxycarboxylic acids that are the required starting materials for the process of Collett. The motivation would

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have been to overcome the need, in Collett's process, for a resolution step. By employing the process of Effenberger, the production of the undesired antipode, and the attendant waste of resources, could largely be avoided. Since all references are drawn to the production of the same ultimate products and specifically teach the necessary elements there would have been a reasonable expectation for success.

Claim Objections

7. Claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

8. Claim 22 is drawn to allowable subject matter. The following is a statement of reasons for the indication of allowable subject matter: The use of methylisobutyl ketone as a cosolvent for either the reaction to form the hydroxy acid or its optical purification is neither disclosed nor fairly suggested by the closest prior art of record: Collet et al (Bulletin de la Société Chimique de France 1973, 12, Pt. 2, pages 3330-3334, English translation, pages 1-18) and Effenberger et al (US 4,859,784 08-1989) or their combination.

Conclusion

9. Claims 11-14 and 16-23 remain pending. Claims 11-14, 16-21 and 23 are rejected. Claim 22 is objected to.

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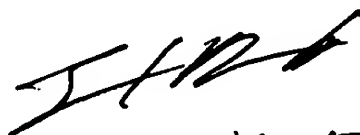
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker
Patent Examiner
Technology Center 1600

May 12, 2003



ACTING FOR

Johann Richter, Ph.D., Esq.
Supervisory Patent Examiner
Technology Center 1600